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RD2007-07

Registration Decision

Bacillus subtilis **strain MBI 600**

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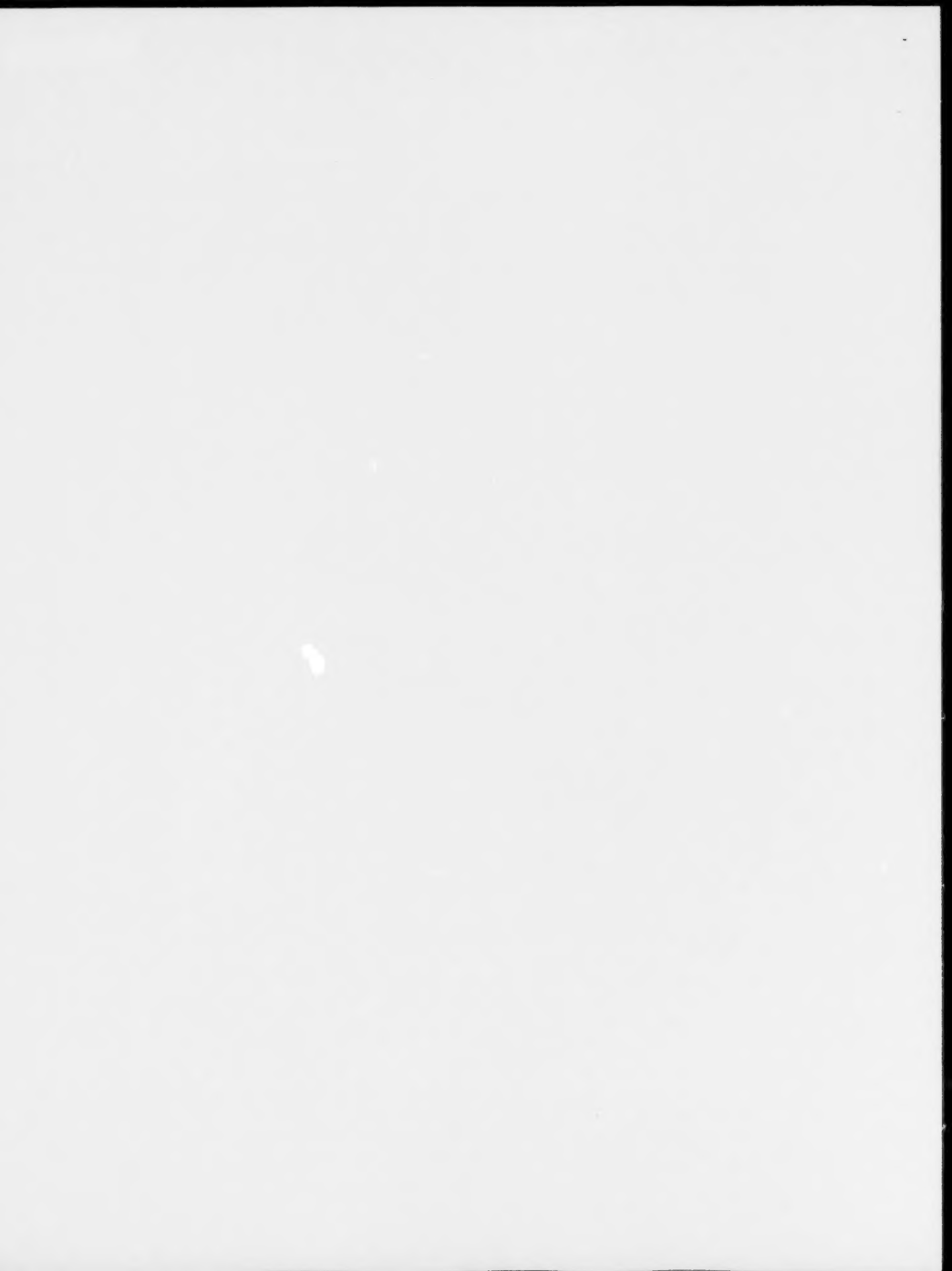
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Registration Decision for *Bacillus subtilis* strain MBI 600

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of technical grade active ingredient *Bacillus subtilis* MBI 600 Technical containing the microbial pest control agent *Bacillus subtilis* strain MBI 600, the manufacturing-use product Subtilex™ Biological Fungicide and the end-use products Pro-Mix (HP, BX, PGX and TA) with Biofungicide to suppress damping-off and root-rot diseases caused by *Pythium* spp. on greenhouse vegetables, including transplants and greenhouse ornamentals.

Current scientific data from the registrant, scientific reports and information from other regulatory agencies were evaluated to determine if, under the proposed conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document¹: Proposed Registration Decision—*Bacillus subtilis* strain MBI 600 (PRD2007-05). This Registration Decision² describes this stage of the PMRA's regulatory process for *Bacillus subtilis* MBI 600 Technical, the manufacturing-use product Subtilex™ Biological Fungicide and the end-use products Pro-Mix (HP, BX, PGX and TA) with Biofungicide and summarizes the Agency's decision and the reasons for it. The PMRA received no comments on Proposed Registration Decision—*Bacillus subtilis* strain MBI 600 (PRD2007-05) that would impact the risk assessment. This decision is consistent with the proposed registration decision stated in Proposed Registration Decision—*Bacillus subtilis* strain MBI 600 (PRD2007-05).

For more details on the information presented in this Registration Decision, please refer to the Science Evaluation section of the related Proposed Registration Decision—*Bacillus subtilis* strain MBI 600 (PRD2007-05).

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable if there is reasonable certainty that no harm to human health, future generations or the

¹ "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

² "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

environment will result from use or exposure to the product under its conditions or proposed conditions of registration³. The Act also requires that products have value⁴ when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (e.g. children) as well as organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at www.pmra-arla.gc.ca.

What Is Pro-Mix With Biofungicide?

The four Pro-Mix with Biofungicide end-use products (HP, BX, PGX and TA) are peat-based soilless growing media that contain the biological pesticide, *Bacillus subtilis* strain MBI 600. *Bacillus subtilis* strain MBI 600 is a naturally occurring bacterium that rapidly colonizes the roots of growing plants and produces an antibiotic protein that suppresses the ability of *Pythium* spp. to grow and reach levels necessary to trigger damping-off or root-rot diseases. The four products are formulated for different uses by greenhouse growers.

Pro-Mix BX with Biofungicide is a general purpose peat-based professional growing medium designed for the cultivation of a wide variety of horticultural plants including vegetable transplants.

Pro-Mix HP with Biofungicide is a highly porous peat-based professional growing medium designed for the cultivation of a wide variety of horticultural plants including water sensitive crops, the propagation of plant cuttings and/or use in low-light conditions.

Pro-Mix PGX with Biofungicide is a peat-based professional growing medium designed for the germination of ornamental and vegetable seeds with plug systems.

Pro-Mix TA with Biofungicide is a general purpose peat-based professional growing medium designed for the germination and growth of tobacco as well as other vegetable and ornamental transplants.

³ "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

⁴ "Value" as defined by subsection 2(1) of *Pest Control Products Act*: "...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and c) health, safety and environmental benefits and social and economic impact".

Health Considerations

Can Approved Uses of Pro-Mix with Biofungicide Affect Human Health?

***Bacillus subtilis* strain MBI 600 is unlikely to affect your health when Pro-Mix with Biofungicide is used according to the label directions.**

Exposure to *Bacillus subtilis* strain MBI 600 may occur during handling of Pro-Mix with Biofungicide (soilless growing media). When assessing health risks, several key factors are considered: the microorganism's biological properties (e.g. production of toxic byproducts), reports of any adverse incidents; its potential to cause disease or toxicity as determined in toxicological studies and the likely levels to which people may be exposed relative to exposures already encountered in nature to other strains of the microorganism. Toxicology studies in laboratory animals describe potential health effects from large doses in hopes of identifying any potential to cause disease or toxicity. No significant toxicity and no signs of causing diseases were observed when *Bacillus subtilis* strain MBI 600 was tested on laboratory animals.

Residues in Water and Food

Dietary risks from food and water are not of concern.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Bacillus subtilis strains are common in nature and the use of Pro-Mix with Biofungicide as growing medium for plants is not expected to significantly increase the natural environmental background levels of this microorganism. Few, if any, bacteria are expected to remain as residues on plants at harvest because *Bacillus subtilis* strain MBI 600 is present in the plant's growing medium. Some strains of *Bacillus subtilis* have been isolated from food samples implicated in food poisoning; however, these strains demonstrated the ability to produce a highly heat-stable toxin that may be similar to a toxin produced by *Bacillus cereus*, a known food borne pathogenic microorganism. *Bacillus subtilis* strain MBI 600 is not reported to produce this toxin. Also, no such effects were reported for this microorganism in the United States where it has been registered since 1994. Furthermore, there was no significant toxicity and no signs of causing diseases were observed when *Bacillus subtilis* strain MBI 600 was administered orally to rats. The establishment of an MRL is therefore not required for *Bacillus subtilis* strain MBI 600. Furthermore, the likelihood of residues of *Bacillus subtilis* strain MBI

600 contaminating drinking water supplies is negligible to non-existent. Consequently, dietary exposure and risk are minimal to non-existent.

Occupational Risks From Handling Pro-Mix With Biofungicide

Occupational risks are not of concern when Pro-Mix with Biofungicide is used according to the label directions, which include protective measures.

Growers handling Pro-Mix with Biofungicide can come into direct contact with *Bacillus subtilis* strain MBI 600 on the skin, in the eyes or by inhalation. For this reason, the label specifies that growers exposed to Pro-Mix with Biofungicide must wear waterproof gloves, a long-sleeved shirt, long pants, shoes and socks. Handlers must also wear a dust-filtering mask and eye goggles when opening bags of product and/or filling potting machines. Furthermore, early-entry workers will be restricted from entering areas where dry Pro-Mix with Biofungicide was handled for a period of up to four hours unless wearing the appropriate personal protective equipment.

For bystanders, exposure is expected to be much less than that of handlers and mixer/loaders and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Pro-Mix with Biofungicide Is Introduced Into the Environment?

Environmental risks are not of concern.

In published literature, other strains of *Bacillus subtilis* have been reported to cause infections in mammals, terrestrial insects and plants. However, these reports were few in number despite the large amount of published literature on this microorganism and either involved unusual strains or the ability of the select strain of *Bacillus subtilis* to cause disease was not thoroughly investigated. There are no published reports of disease associated with *Bacillus subtilis* in birds, earthworms, bees, aquatic invertebrates, fish, algae and aquatic plants. *Bacillus subtilis* is not generally considered to be a disease causing agent. Therefore, Pro-Mix with Biofungicide is expected to present a negligible risk to non-target organisms.

Value Considerations

What Is the Value of Pro-Mix With Biofungicide?

The four Pro-Mix with Biofungicide end-use products suppress damping-off and root-rot diseases caused by *Pythium* spp. on greenhouse crops. The use of these products as seeding or planting media will replace the first preventative fungicide application; thus, it may reduce the number of applications of chemical fungicides. This reduction in the number of applications could decrease the possibility of pathogens developing resistance to traditional chemical-based fungicides. These four end-use products can also potentially enhance the adoption of reduced-risk technologies by producers because they are ready for immediate use, have a long shelf-life (up to 24 months) and offer few risks to human health and the environment.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the label of Pro-Mix with Biofungicide to address the potential risks are as follows.

- **Human Health**

Because of concerns with toxicity via the pulmonary route and with users developing allergic reactions through repeated high exposures to *Bacillus subtilis* strain MBI 600, anyone handling Pro-Mix with Biofungicide must wear waterproof gloves, long-sleeved shirt, long pants and shoes plus socks. A dust/mist-filtering mask must also be worn when opening bags and/or filling potting machines. Furthermore, early-entry workers will be restricted from entering areas where dry Pro-Mix with Biofungicide was handled for a period of up to four hours unless wearing the appropriate personal protective equipment.

- **Environment**

As a general precaution, handlers are asked to not contaminate irrigation or drinking water or aquatic habitats by cleaning of equipment or by disposing of wastes. In addition, growers must not allow effluent or runoff from greenhouses containing this product to enter lakes, streams, ponds or other water bodies.

Other Information

The relevant test data on which the decision is based (as referenced in this document) are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

Any person may file a notice of objection⁵ regarding this registration decision on *Bacillus subtilis* strain MBI 600 within 60 days from the date of publication of this Registration Decision Document. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the PMRA's website (Request a Reconsideration of Decision, www.pmra-arla.gc.ca/english/pubreg/reconsideration-e.html) or contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

⁵ As per subsection 35(1) of the *Pest Control Products Act* (<http://laws.justice.gc.ca/en/P-9.01/92455.html>).

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1.0 THE ACTIVE INGREDIENT, ITS PROPERTIES AND USES

- | | |
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| PMRA 1099753 | International Regulatory Status of the <i>Bacillus subtilis</i> MBI 600 Technical. Premier Horticulture. 2005. DACO: M1.3 |
| PMRA 1098379 | Product profile and proposed use pattern Subtilex™ Biological Fungicide. Premier Horticulture. 2005. DACO: M1.2 |
| PMRA 1098380 | International Regulatory Status Subtilex™ Biological Fungicide. Premier Horticulture. 2005. DACO: M1.3 |
| PMRA 1098404 | Product profile and proposed use pattern PRO-MIX HP with Biofungicide. Premier Horticulture. 2005. DACO: M1.2 |
| PMRA 1098405 | International Regulatory Status PRO-MIX HP with Biofungicide. Premier Horticulture. 2005. DACO: M1.3 |
| PMRA 1098448 | Product profile and proposed use pattern PRO-MIX BX with Biofungicide. Premier Horticulture. 2005. DACO: M1.2 |
| PMRA 1098449 | International Regulatory Status PRO-MIX BX with Biofungicide. Premier Horticulture. 2005. DACO: M1.3 |
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PMRA 1099763	Results of API test Kit. 2004. DACO: M2.7.1
PMRA 1099764	Reconnaître la souche de <i>Bacillus subtilis</i> MBI 600 parmi différentes souches de <i>Bacillus</i> sp. Premier Horticulture. 2005. DACO: M2.7.1
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B. ADDITIONAL INFORMATION CONSIDERED**i) Published Information****2.0 METHODS OF ANALYSIS**

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